IRB Approved at the Study LevelDec 07, 2020 #29331253.0

**Plenitude Study: Safety and Efficacy of a THC/CBD study drug for Improving Uncontrolled Pain Relief in Patients with Advanced Cancer: A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study**

Dear Dr. \_\_\_\_\_\_\_\_,

We are recruiting adult men and women with advanced cancer pain and uncontrolled pain relief residing close to the practice of **Dr. Suzanne Sisley**, located at the **Scottsdale Research Institute, 5436 E Tapekim Rd, Cave Creek, AZ 85331** for an upcoming clinical research study The study aims to reduce cancer-related pain and improve quality of life by verifying the effectiveness of vaporized pharmaceutical grade cannabis (PPP001)

Eligibility:

* 18 years of age or older and able to provide written informed consent in English or Spanish.
* The patient must have a diagnosis of advanced cancer (stage 3 or later) for which there is no known curative therapy.
* Patient is experiencing at least 2 symptoms related to cancer (including pain).
* Patient cannot have any clinical interventions planned.
* If the patient is taking concomitant medication for pain, they must be on a stable dose (the use of concomitant pain medication is allowed in the study if stabilized before baseline including 3x10% of the total morphine equivalent daily dose (MEDD) as rescue medication. In addition, NSAID and acetaminophen will be able to be added as analgesics for the 4-week treatment period). The patient does not have to have prior experience with marijuana, and they do not have to be marijuana-naïve to take part in the study. If the patient is an occasional cannabis user (Cannabis use in any form: 1-3 times/week) he or she must agree to a 7-day washout period where they will refrain from any cannabis use. After 1-week of cannabis abstinence, THC blood levels will be verified, and results must be negative, or the patient won’t be randomized in the study.
* The patient must designate a caregiver to accompany him/her to the clinical site, assist him/her during the Main and Open Label Long Term Follow-Up phase, fill out a caregiver questionnaire at specific visits and return/retrieve study treatment at the site during the Open Label Long Term Follow-Up phase.

This study is a 1-year study including a 4-week randomized, double-blind, placebo-controlled, parallel group design trial to evaluate the safety and efficacy of an inhaled THC/CBD study drug in **patients with uncontrolled symptoms related to advanced incurable cancer**. Primary and secondary endpoints will be determined using subject and caregiver facing scales throughout the course of the study. The 4-week double blind treatment phase will be followed by a long-term follow up phase in open label for the remainder of the year so all subjects, including patients previously under placebo, will receive active treatment post the initial 4 weeks.

The inhalation of the THC/CBD study drug or placebo using a vaporizer will be instructed three times a day at 4-6-hour intervals. Concomitant medication will be allowed if stabilized before baseline. The patient will be trained on the inhalation procedure at the screening visit at the clinical site.

At **baseline visit**, a study staff member will perform study procedures (physical exam, vital signs, ECG, Blood sampling for cannabinoid concentration level, hematology and chemistry) and make sure the treatment is inhaled properly at the patient’s capacity (without any dizziness, nausea, vomiting, panic or difficulty breathing). Patients will have a dose titration period during the first week with daily phone calls, followed by an additional 3-week stable dose period of treatment. The dose escalation will allow patients to adapt to the potential AEs of cannabinoids.

The **end of Double-Blind Treatment Period visit** will be performed at week 4.

Once the patient has completed the 4 weeks of inhaled PPP001 or placebo of the study main phase, he ∕ she will be enrolled into a long-term follow-up phase (1-year maximum period). All patients, including the ones in the placebo group, will receive the active treatment during the long-term follow-up phase of the study. A new dose escalation with phone calls on a daily basis will be performed for all patients allowing patients previously under placebo to adapt to the potential AEs of cannabinoids and transaminases/bilirubin/creatinine will be carefully followed with additional laboratory tests if necessary.

The patient MUST have a Caregiver to be in the study. A caregiver is someone who lives with the patient or who has contact with the patient for a sufficient amount of time each week/daily (eg, a friend, family member, or spouse), and who is able to support the patient for the duration of the study. The caregiver will be required to assist with the patient’s compliance with the study requirements, attend and accompany the patient to/from study visits (car, bus, taxi), and assess the patient’s condition throughout the study. The caregiver will be asked to sign a separate informed consent form. If they decide to stop serving as the patient’s caregiver in this research study, the patient will no longer be able to continue their participation unless another caregiver is found, who can adhere to the requirements of the study.

We would appreciate your referring or calling to discuss any participant you think might be suitable for this study.

Please do not hesitate to contact me at suesisleymd@sriresearch.org or by phone at 480-326-6023 for additional information about the study.

Sincerely,

Suzanne Sisley, MD